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Photochemical deprotection of nitro-substituted benzenesulfenates via photoinduced electron transfer

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Abstract—The photochemical deprotection of alkyl 2,4-dinitrobenzenesulfenate or alkyl 2-nitrobenzenesulfenate was successfully achieved by addition of triethylamine, while it was unsuccessful without triethylamine. The sulfur–oxygen bond cleavage is thought to occur heterolytically in the sulfenate anion radical produced by photoinduced electron transfer with triethylamine.
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Selective protection and deprotection of specific functional groups are fundamental procedures in multi-step organic syntheses. Among various deprotection methods, photochemical deprotection is attractive because it minimizes the use of additional reagents, can be controlled simply by switching on a light, and can be applied to photofunctional materials. The 2,4-dinitrobenzenesulfenyl group is known to be useful in the protection of hydroxy groups.[1] In addition to deprotection by conventional procedures, this protecting group can also be removed photochemically, absorbing in the near-ultraviolet to visible light region (<450 nm). As early as the 1960s, Barton and his co-workers reported efficient deprotection of 2,4-dinitrobenzenesulfenyl carboxylate by photochemical cleavage of the sulfur–oxygen bond to obtain the corresponding carboxylic acid.[2–4] They suggested that cleavage occurred by an ionic mechanism. The equivalent protected alcohols, that is, alkyl 2,4-dinitrobenzenesulfenates, however, are less reactive under the same photochemical conditions except for the benzyl derivative. The 4-nitrobenzenesulfenyl group is more sensitive to light than for the dinitro group, including in the case of alcohols. However, the sulfur–oxygen bond in this substrate tends to cleave homolytically, and thus generates β-fission products (a carbonyl compound and an alkyl radical) besides the alcohols. Unsubstituted benzenesulfenate
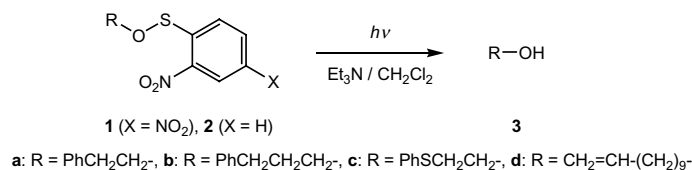
also reacts photochemically but is moderately unstable thermally.[5]

With the aim of avoiding generation of the alkoxyl radical, we have investigated sulfur–oxygen bond cleavage in the photochemically generated anion radical, which can transform to a sulfenyl radical and an alkoxide anion. Several applications of photoinduced electron transfer (PET) have been reported for deprotection, for example reductive cleavage of sulfonates and sulfonamides.[6,7] Triethylamine can be used as an electron donor to enable photoreduction of carbonyl compounds as well as for carbon–oxygen bond cleavage of α-oxygenated ketones.[8–11] We report herein the efficient photochemical deprotection of alkyl 2,4-dinitrobenzenesulfenate by the addition of triethylamine.

Sulfenates **1** and **2** (Scheme 1) were prepared by reaction of the corresponding alcohol with (di)nitrobenzenesulfenyl chloride by a literature method.[12] Characteristic absorption bands of 2,4-dinitrobenzenesulfenyl and 2-nitrobenzenesulfenyl groups were observed in near-ultraviolet to visible region in dichloromethane: for example, for **1d**, $\lambda_{max} = 339$ nm ($\varepsilon = 9.5 \times 10^3\,cm^{-1}\,dm^3\,mol^{-1}$), 390 nm (shoulder); for **2d**, 400 nm ($\varepsilon = 3.5 \times 10^3\,cm^{-1}\,dm^3\,mol^{-1}$). When a dichloromethane solution containing **1a** ($0.01\,mol\,dm^{-3}$) in a Pyrex tube was irradiated ($\lambda > 280$ nm, 12 h) using a 500-W super-high-pressure mercury lamp under argon atmosphere, the alcohol was not obtained and **1a** was almost completely recovered (86%), as has been previously reported.[2–4] Under these conditions, the major product was a rearranged product, the sulfoxide **4a**

1 (X = NO$_2$), **2** (X = H)　　　　　　　**3**

a: R = PhCH$_2$CH$_2$-, **b**: R = PhCH$_2$CH$_2$CH$_2$-, **c**: R = PhSCH$_2$CH$_2$-, **d**: R = CH$_2$=CH-(CH$_2$)$_9$-

Scheme 1.

(14%). Previously, it was reported that the unsubstituted benzenesulfenate did not rearrange to the sulfoxide photochemically.[13] The details of this rearrangement will be discussed in another paper. On the other hand, under the same conditions except for addition of triethylamine (1% vs. dichloromethane), the deprotected alcohol (**3**) was afforded in high yield (Table 1) and no β-fission products were obtained. Highly polar materials were detected, probably compounds related to sulfonic or sulfinic acid; the fate of the dinitrobenzenesulfenyl part remains unclarified. Since the excess amount of triethylamine could be removed by evaporation, the alcohol **3** was easily isolated by subsequent chromatography. In the dark, **1a–d** were unchanged after 10h in triethylamine solvent. Furthermore, **1a–d** were completely recovered after heating in acetic acid at 100°C for 30min.


4 (X = NO$_2$), **5** (X = H)
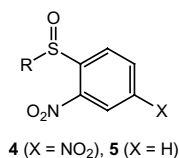
The 2-nitro derivative (**2**), when irradiated in the presence of triethylamine, also yielded similar results but was less reactive than the dinitro derivative **1** (Table 1). At present, we consider this to result from the weaker light absorptivity and electron-accepting ability of **2** compared to **1**. Irradiation of **2a** without triethylamine afforded sulfoxide **5a** (16% after irradiation for 12h) but the recovery of **2a** (30%) was reduced compared to that of **1a**. Similarly to **1**, compound **2** was stable both in triethylat room temperature and in hot acetic acid.

To gain insight into the electronic properties and energies of the anion radicals of **1** and **2**, we performed the density functional theoretical (DFT) calculations.[14] Methyl sulfenates (**1e**, **2e**) were selected as model molecules, and unsubstituted benzenesulfenate (**6**) and methanesulfenate (**7**) were also calculated for comparison.

Table 1. Photodeprotection of the sulfenates (**1**, **2**) with triethylamine[a]

Substrate	Irradiation time (h)	Yield of alcohol **3** (%)[b]
1a	7	94
1b	9	99
1c	5.5	93
1d	7	97
2a	21	95
2b	28	99
2c	14	93
2d	23	99

[a] Reaction conditions described in text.
[b] Determined by isolation.

1e　　　**2e**

6　　　**7**
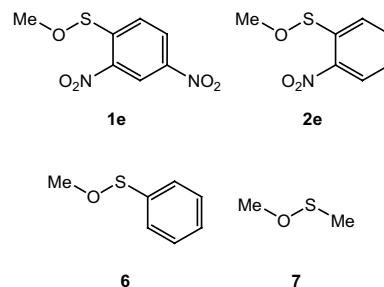
First, the possibility of the electron transfer was estimated as follows. Calculated (B3LYP/6-31+G*) electron affinities of the excited triplet states of **1e**, **2e**, and nitrobenzene were 4.21, 3.57, and 3.64eV, respectively; the experimental literature value for nitrobenzene is 3.52eV.[15–17] These values indicate that sulfenates **1e** and **2e** are comparable electron acceptors to nitrobenzene. Electron transfer from triethylamine to the excited triplet of nitrobenzene is estimated to be exothermic by the Weller equation when inputting experimental values,[16,18,19]† thus electron transfer to **1e** or **2e** is also considered feasible.

Next, geometries and electronic properties of the anion radicals were investigated. The LUMOs of **6** and **7** are assigned as antibonding σ-orbitals on the sulfur–oxygen bond, and as expected the sulfur–oxygen bond in those anion radicals is extremely elongated compared to the neutral molecules (Table 2). Thus bond dissociation may occur simultaneously with electron attachment. For the anion radicals of **6** and **7** both the sulfur atom and methoxy group are calculated to have moderate spin density as well as negative charge.

For the anion radicals of **1e** and **2e**, elongation of the sulfur–oxygen bond occurred to a lesser extent. The spin densities on both the sulfur atom and the methoxy group are calculated to be nearly zero, thus the spin is localized on the (di)nitrophenyl group in **1e** and **2e**. Additionally, the 2-nitro group in the anion radical of **1e** is more negatively charged and has more spin density than the 4-nitro group: the charges are calculated to be −0.74 (2-NO$_2$) and −0.39 (4-NO$_2$), and the spin densities are 0.68 (2-NO$_2$) and 0.06 (4-NO$_2$). The charges of

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† When the experimental values of +1.15,[16] −1.10,[18] and 2.52eV[16] are input as the oxidation potential of triethylamine (E_{ox} vs. SCE in acetonitrile), the reduction potential of nitrobenzene (E_{red} vs. SCE in acetonitrile) and the triplet energy (E_T) of nitrobenzene, respectively, the free energy difference of the electron transfer ($\Delta G = E_{ox} - E_{red} - E_T + C$)[19] is calculated to be −0.11eV for the Coulombic correction term (C) in dichloromethane of +0.16eV.

Table 2. Optimized S–O bond length, charge, and spin[a]

|		r (S–O)(Å)	Charge		Spin	
			S	OMe	S	OMe
1e	Anion radical	1.777	+0.64	−0.48	0.01	0.00
	Neutral	1.692	+0.73	−0.38		
2e	Anion radical	1.783	+0.58	−0.49	0.03	0.00
	Neutral	1.698	+0.69	−0.39		
6	Anion radical	2.536	−0.13	−0.47	0.48	0.52
	Neutral	1.692	+0.56	−0.37		
7	Anion radical	2.508	−0.27	−0.56	0.55	0.44
	Neutral	1.695	+0.48	−0.38		

[a] Calculations were performed using B3LYP functional and 6-31+G* basis set. Charge and spin were obtained by natural population analysis.
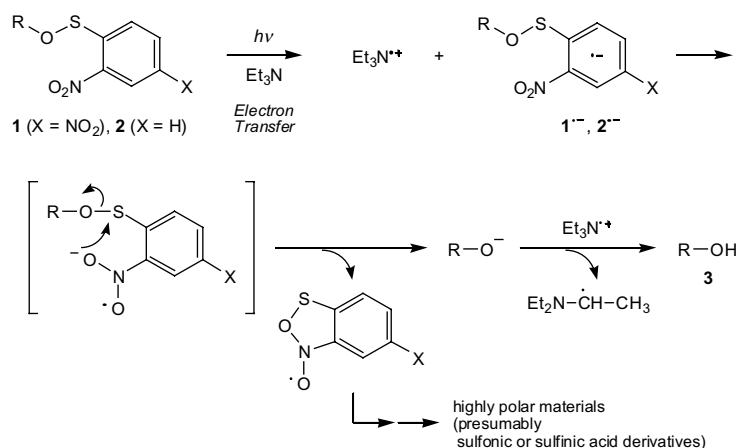
Scheme 2.

the both nitro groups in the anion radical are more negative than those in the neutral **1e** (−0.26 for 2-NO$_2$ and 4-NO$_2$). In contrast to **6** and **7**, the sulfur atom is positively charged as in the neutral molecules. The lower unoccupied orbitals of neutral **1e** and **2e** are assigned to π-orbitals spread over the benzene ring and the nitro group(s), and the antibonding σ-orbital on the sulfur–oxygen bond appears at a higher lying MO: LUMO+3 (**1e**) and LUMO+2 (**2e**). Therefore, cleavage of the anion radicals **1** and **2** is expected to occur heterolytically as in the neutral molecules rather than homolytically. This is consistent with β-fission products not being produced.

A possible mechanism of this reaction is presented in Scheme 2. The excited triplet state of **1** or **2** is rapidly quenched by triethylamine to afford the anion radical of **1** or **2** and the triethylamine cation radical. The nucleophilicity of the oxygen atom of the 2-nitro group in the anion radical is increasing compared to the neutral molecule. Therefore, intramolecular nucleophilic attack of the oxygen atom of the 2-nitro group may assist the cleavage of the sulfur–oxygen bond to produce the alkoxide anion, followed by α-proton transfer from the triethylamine cation radical to the alkoxide anion.

Similarly to photoreduction of nitrobenzenes with triethylamine,[20,21] an α-proton of the triethylamine cation radical can transfer to the 2-nitro group in **1**·⁻ or **2**·⁻. Although this possibility cannot be excluded, the sul-
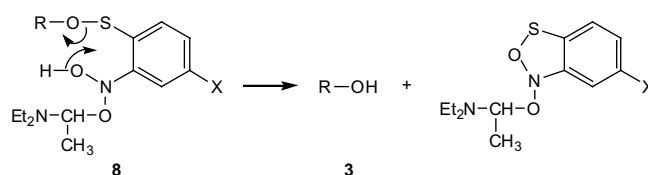
Scheme 3.

fur–oxygen bond cleavage in the coupling product **8** from the resulting radical pair (Scheme 3) may need more activation energy than that in the anion radical **1**·⁻ or **2**·⁻.

In summary, photochemical deprotection of alkyl 2,4-dinitrobenzenesulfenate was successfully achieved by addition of triethylamine. The sulfur–oxygen bond cleavage is thought to occur heterolytically in the sulfenate anion radical produced by photoinduced electron transfer with triethylamine.

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